AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A method of detecting, quantifying, and distinguishing between sequence variants with regards to one or several target sequences in a sample, wherein a target nucleic acid sequence in a sample ~~by contacting the sample~~ is placed in contact with a probe to hybridize the probe to the target sequence, and detecting the hybridized probe, wherein said probe having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing to two at least substantially neighboring regions of the target sequence, comprising the following steps:

a) hybridizing the target sequence to the probe ends under hybridizing conditions;

b) covalently connecting the ends of the hybridized probe with each other to form a circularized structure;

wherein the probe is provided indirectly or directly with a solid phase anchor (A or A through E) and with a cleavable (B) and a detectable function (C), or a dissociable (D, F) and detectable function (C), in such a way that the detectable

function (C) remains linked to the solid phase if the target has interacted with the probe;

and the method comprises the further steps of:

c) cleaving said cleavable function (B) if present;

d) separating detectable functions no longer linked to said solid phase; and

e) detecting the presence and, if desired, location of the remaining probe as indicative of the presence of the target nucleic acid sequence.

2. (original) The method according to claim 1, wherein said detectable function is cleaved by cleaving a cleavable linker located on the same probe end as the detectable function.

3. (previously presented) The method according to claim 1, wherein one or both of the probe ends have at least two branches, and a detectable function is provided on each of the branches on one end part of the probe, the detectable functions being different and distinguishable from each other.

4. (previously presented) The method according to claim 3, wherein one probe end is linear and the other probe end is branched.

5. (original) The method according to claim 1, wherein said detectable function is dissociable by being provided on a circular probe hybridizing to said target-specific probe.

6. (original) The method according to claim 1, wherein said detectable function is dissociable by being provided on said target-specific probe hybridizing to a circular probe.

7. (original) The method according to claim 1, wherein said target-specific probe is designed to hybridize to the target molecule to leave an interspace between the probe ends, at least one additional probe is provided which is designed to hybridize to the target molecule in said interspace, and the hybridized probes are covalently interconnected.

8. (original) The method according to claim 1, wherein said target-specific probe or probes are designed to hybridize to the target molecule to leave a small gap between adjacent probe ends, and said gap or gaps are filled by an extension reaction prior to covalently interconnecting the probe ends.

9. (previously presented) The method according to claim 1, wherein said covalent connection of the probe ends is performed by enzymatic, ribozyme-mediated or chemical ligation.

10. (original) The method according to claim 1, wherein said target molecule is a DNA or RNA sequence.

11. (original) The method according to claim 1, wherein said probe or probes are oligonucleotides.

12. (original) The method according to claim 1, wherein said probe or probes are immobilized to a solid phase.

13. (original) The method according to claim 1, wherein said target sequence is immobilized to a solid phase.

14-21. (cancelled)

REMARKS

At the outset, applicant would like to thank the Examiner for his time and consideration of the present application at the interview of September 11, 2003 with the undersigned agent. At the interview, the issues raised in the outstanding Official Action were discussed. In addition, the Examiner and the undersigned agent discussed potential changes to the claims.

Claims 1-13 are pending in the present application. Claim 1 has been amended to recite a method of detecting, quantifying, and distinguishing between sequence variants with regards to one or several target sequences in a sample. This recitation is supported in the present specification at page 4, lines 35-39. Applicant would like to thank the Examiner for his suggestion for adding this recitation to claim 1. It is believed that the present application is in condition for allowance.

In the outstanding Official Action, claims 1, 5, 6, and 9-13 were rejected under 35 USC §102(b) as allegedly being anticipated by NILSSON et al. (Science, Vol. 265, pages 2085-2088, September 30, 1994). This rejection is respectfully traversed.

Applicant respectfully submits that NILSSON et al. fail to disclose or suggest the claimed invention. In the NILSSON et al. publication, padlock probes are used for localization and

detection of a specific segment of a single stranded DNA. A padlock probe is defined as an oligonucleotide probe for localized detection of specific nucleic acids composed of two target-complementary end-segments connected by a linker. The padlock probe is added to a solid phase anchored single-stranded DNA.

However, the padlock probe is not provided with a cleavable function or a dissociable detectable function. The padlock probe is hybridized to and circularized on a segment of a single-stranded DNA of interest.

Contrary to the assertions of the Official Action, non-ligated probes are not removed by cleaving the probe. Indeed, they do not even contain a cleavable function. The probes are removed because they are not linked to the target sequence.

In addition, the probes do not contain a solid phase anchor. They become anchored to the probes only if they are ligated in a target sequence dependent manner. This nucleic acid sequence can be read by use of detectable markers linked to the padlock probe.

In the present invention, the padlock probe is anchored to a solid phase, to which the nucleic acid sequence to be analyzed is added. A detectable marker is linked to the padlock probe. The padlock probe may also contain a cleavable segment (see Figure 1). The nucleic acid-containing sample is added to

the anchored probe and a segment, the target sequence, of the nucleic acid sequence is hybridized to the complementary end-segments of the padlock probe, and the padlock probe becomes circularized through ligation of the ends. Padlock probes that are not hybridized to a nucleic acid sequence are cleaved in a way that the detectable marker is removed together with the dissociable segment. These dissociable segments are removed by washing. As to the solid phase, padlock probes which have interacted with a nucleic acid sequence from the sample can easily be detected through analysis of the detectable marker.

In view of the above, it is believed that NILSSON et al. do not anticipate or render obvious the claimed invention.

In the outstanding Official Action, claims 2-4 were rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of URDEA et al. 5,124,246. Claims 7-8 were then rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of BIRKENMEYER et al. 5,427,930.

However, applicant respectfully submits that URDEA et al. do not remedy the deficiencies of the NILSSON et al. publication for reference purposes relative to the present claims. URDEA et al. relate to amplifying a signal in biochemical assays by using linear or branched oligonucleotide multimers. However, URDEA et al. do not teach a method of

detecting, quantifying, and distinguishing between sequence variants with regards to one or several target sequences in a sample. As a result, it is believed that the proposed combination of NILSSON et al. in view of URDEA et al. fails to render obvious the claimed invention.

As to the BIRKENMEYER et al. publication, BIRKENMEYER et al. disclose a Ligase Chain Reaction assay. BIRKENMEYER et al. do not teach a method of detecting, quantifying, and distinguishing between sequence variants with regards to one or several target sequences in a sample. Applicant respectfully submits that BIRKENMEYER et al. fail to remedy the deficiencies of NILSSON et al. It is believed that the proposed combination of NILSSON et al in view of BIRKENMEYER et al. fail to disclose or suggest the claimed invention.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 1-13, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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